Pharmacy Drug Policy

SUBJECT: Kresladi (marnetegragene autotemcel)
POLICY NUMBER: PHARMACY-139
EFFECTIVE DATE: 09/2026
LAST REVIEW DATE: 09/24/2026

If the member's subscriber contract excludes coverage for a specific service or prescription drug, it is not covered under that contract. In such cases, medical or drug policy criteria are not applied. This drug policy applies to the following line/s of business:

Policy Application

Category:	☒ Commercial Group (e.g., EPO, HMO, POS, PPO)	☒ Medicare Advantage
	☒ On Exchange Qualified Health Plans (QHP)	☐ Medicare Part D
	☒ Off Exchange Direct Pay	☒ Essential Plan (EP)
	☒ Medicaid & Health and Recovery Plans (MMC/HARP)	☒ Child Health Plus (CHP)
	☐ Federal Employee Program (FEP)	☐ Ancillary Services
	☒ Dual Eligible Special Needs Plan (D-SNP)	

DESCRIPTION:

Leukocyte adhesion deficiency (LAD) syndromes are a group of rare disorders affecting the immune system and are characterized by defects affecting how leukocytes respond and migrate to wound or infection sites. There are three subtypes of this primary immunodeficiency disease: LAD I is caused by mutations of the ITGB2 gene, LAD II is caused by mutations of the SLC35C1 gene, and LAD III is a mutation in the gene for Kindlin 3. Severity and symptoms vary person to person however all affected individuals develop an increased susceptibility to developing recurrent bacterial and fungal infections. In infants, umbilical cord complications (delayed separation and omphalitis), impaired wound healing, and persistent Leukocytosis is common in LAD-I. Patients with severe cases of LAD-I express 2% of normal levels of CD18-expressing neutrophils.

Specifically addressing LAD-I, the estimated prevalence is one case per one million people and those afflicted with a severe form carry a significant mortality risk (> 60%) in those under two who do not receive a stem cell transplant. Hematopoietic Stem Cell Transplant is the only curative treatment for this condition and requires one to match with a donor.

Kresladi (marnetegragene autotemcel) is a gene therapy containing autologous hematopoietic stem cells that have been genetically modified with a lentiviral vector to deliver a functional copy of the ITGB2 gene (targeting those with LAD-I). Mechanistically, this therapy functions to deliver the gene encodes the beta-2 integrin component CD18, a key protein that facilitates leukocyte adhesion and enables extravasation from blood vessels to fight infection. In addition to stem cell collection, treatment with Kresladi requires myeloablative conditioning prior to infusion, as well as inpatient monitoring post infusion.

In its October 3, 2023, press release, Rocket Pharmaceuticals reported that in a Phase 1/2 Kresladi demonstrated 100% overall survival at 12 months post infusion (and for the entire duration of follow-up) for all nine patients with LAD-I with 12 to 24 months of available follow-up. These nine subjects were between five months and nine years of age. Results from the trial also showed large decreases compared with pre-treatment history in the incidences of significant infections, combined with evidence of resolution of disease-related skin lesions and restoration of wound repair capabilities. In a relative comparator, results from a 2021 multicenter, retrospective study of data collected from 84

patients with LAD-I and -III who received allogeneic HSCT between 2007 and 2017 demonstrated a three-year overall survival of 83%.

On March 26, 2026, the FDA granted accelerated approval to Kresladi. The safety and effectiveness of Kresladi were established in an open-label study in nine pediatric patients with molecularly confirmed ITGB2-associated, severe LAD-I. All of the patients received Kresladi as a single IV infusion at a median dose of 4.3 × 106 CD34+ cells/kg (range: 2.8 to 10 × 106 CD34+ cells/kg). Kresladi increased key biomarker (CD18 and CD11a) expression 12 months post-infusion, with sustained effects through 24 months post-infusion. All nine patients enrolled in the pivotal Kresladi study remained alive through 24 months of follow-up and continue to be followed post-approval.

POLICY:

Kresladi (marnetegragene autotemcel) – Medical Benefit
1. Must be at least 3 months of age **AND** 2. Prescribed by or in consultation with an immunologist, hematologist, or prescriber specializes in the treatment of leukocyte adhesion deficiency (LAD) **AND** 3. Enrollee has confirmed diagnosis of Severe LAD-I as demonstrated by: a. Molecular genetic testing revealing a characteristic mutation in the ITGB2 gene b. Flow cytometry indicating: i. CD18 expression on < 2% neutrophils (polymorphonuclear neutrophils (PMNs)) **OR** ii. CD18+ PMNs are > 2% with < 2% CD11a or CD11b expressing PMNs with documented ITGB2 mutation and clinical history consistent with LAD-I **AND** 4. Enrollee has clinical history supporting Severe LAD-I including: a. Recurrent, often severe, bacterial and/or fungal infections. These infections most often involve the skin and mucous membranes **OR** b. Absence of pus formation at the site of infection **OR** c. For neonates, delayed detachment of umbilical cord along with infection of umbilical cord stump **OR** d. Other indicative conditions include periodontitis and gingivitis **AND** 5. Must have documentation that the patient does not have a human leukocyte antigen (HLA)-identical related donor available for hematopoietic stem cell transplant **AND** 6. The patient must be eligible to undergo hematopoietic stem cell transplant (HSCT) **AND** 7. Patients with any of the following will not be eligible for coverage (documentation, including laboratory results [taken within the past 3 months] is required): a. Hepatic dysfunction defined as bilirubin > 1.5x upper limit of normal (ULN) or alanine aminotransferase (ALT) or aspartate aminotransferase (AST) > 2.5x ULN b. Renal dysfunction as defined by either Grade 3 or higher abnormalities in serum sodium, potassium, calcium, magnesium or phosphate as defined by NCI Common Terminology Criteria for Adverse Events (CTCAE) v5.0, or the requirement for either peritoneal dialysis or hemodialysis c. Pulmonary dysfunction as defined by either: i. Need for supplemental oxygen during the prior 2 weeks (in absence of acute infection) ii. Oxygen saturation (by pulse oximetry) < 90% d. Significant medical conditions, including documented human immunodeficiency virus (HIV) infection, poorly controlled diabetes, poorly controlled hypertension, poorly controlled cardiac arrhythmia or congestive heart failure; or arterial thromboembolic events (including stroke or myocardial infarction) within the 6 prior months **AND** 8. Kresladi is indicated for one-time single-dose intravenous use only and therefore will not be authorized for retreatment. Retreatment will be considered experimental and investigational when

any FDA approved gene therapy, or any other gene therapy under investigation, has been previously administered.
9. Use of Kresladi is considered experimental and investigational when the above criteria are not met.
10. Use of Kresladi to treat other indications will be considered experimental and investigational.
11. Approval will be for 6 months to allow one-time administration

POLICY GUIDELINES:

1. Utilization Management is contract dependent. Refer to specific contract/benefit language for exclusions.
   a. Coverage criteria may be dependent on the contract renewal date.
   b. Coverage of drugs listed in this policy are contract dependent.
   c. Not all contracts/benefits allow coverage of healthcare professional administered drugs as part of their pharmacy benefit
   d. Not all contracts/benefits cover all medical infusible drugs.
2. Clinical documentation must be submitted for each request (initial and recertification [if applicable]) unless otherwise specified (e.g., provider attestation required). Supporting documentation includes, but is not limited to, progress notes documenting previous treatments and treatment history, diagnostic testing, laboratory test results, genetic testing or biomarker results, imaging and other objective or subjective measures of benefit. Requested dosing must remain consistent with FDA-approved dosing recommendations.
3. This policy does not apply to Medicare Part D and D-SNP pharmacy benefits. The drugs in this policy may apply to all other lines of business including Medicare Advantage.
4. Unless otherwise indicated within drug specific criteria, the drugs listed in this policy are administered by a healthcare professional and therefore are covered under the medical benefit.
5. All utilization management requirements outlined in this policy are compliant with applicable New York State insurance laws and regulations. Policies will be reviewed and updated as necessary to ensure ongoing compliance with all state and federally mandated coverage requirements.
6. For commercial contracts, medical necessity determinations align with the Certificate of Coverage issued by the Health Plan, which states that covered services must be clinically appropriate and not primarily for the convenience of the member, the member's family, or the provider.
7. This policy is based on available evidence as of the last review date. Coverage determinations are subject to applicable plan documents, state and federal regulations, and individual patient circumstances. This policy does not constitute medical advice.
8. This policy is subject to ongoing revision. Newly marketed drugs and existing drugs with new indications may be subject to prior authorization until formal coverage criteria are established. Inclusion of a drug in this policy does not guarantee its current availability on the market, as some agents may be discontinued, withdrawn, or otherwise unavailable. As product status changes, drugs may be removed from the policy.
9. For members with Medicare Advantage, medications with a National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) will be covered pursuant to the criteria outlined by the NCD and/or LCD. NCDs/LCDs for applicable medications can be found on the CMS website at https://www.cms.gov/medicare-coverage-database/search.aspx. In the absence of a Medicare National Coverage Determination (NCD), Local Coverage Determination (LCD), or other Medicare coverage guidance, CMS permits a Medicare Advantage Organization (MAO) to establish its own coverage determinations in accordance with 42 CFR § 422.101(b)(6). Indications that have not been addressed by the applicable medication's LCD/NCD will be covered in accordance with criteria determined by the Health Plan. Step therapy requirements may be imposed in addition to LCD/NCD requirements.

10. Manufacturers may either discontinue participation in, or may not participate in, the Medicaid Drug Rebate Program (MDRP). Under New York State Medicaid requirements, physician-administered drugs must be produced by manufacturers that participate in the MDRP. Products made by manufacturers that do not participate in the MDRP will not be covered under Medicaid Managed Care/HARP lines of business. Drug coverage will not be available for any product from a non-participating manufacturer. For a complete list of New/Reinstated & Terminated Labelers please visit: https://www.medicaid.gov/medicaid/prescriptiondrugs/medicaid-drug-rebate-program/newreinstated-terminated-labeler-information/index.html
11. The requested site of care may impact approval timeframe and is subject to review.
12. Approval timeframes may be extended to align authorization periods for drugs administered as part of a multidrug regimen, including when regimen components are administered across different benefits. This provision does not apply when the approval timeframe reflects a drug-specific limitation on duration of therapy.
13. The following applies to all gene and cellular therapies unless otherwise specified within the drug-specific coverage criteria:
    a. Administration, Retreatment, and Treatment with Additional or Other Gene/Cellular Therapies
        i. One-Time Administration
            1. Most gene and cellular therapies, whether autologous, allogeneic ("off-the-shelf"), or in vivo gene-transfer therapies, are designed and studied as one-time treatments.
            2. Repeat dosing, reinfusion, or sequential therapy with other gene or cellular products has not been established as safe, effective, or clinically appropriate.
        ii. Retreatment/Repeat Administration
            1. Retreatment with the same gene or cellular therapy product is considered experimental and investigational because:
                a. Clinical trials evaluated these therapies as single-administration interventions
                b. Safety, efficacy, and durability of a second administration have not been established
                c. Risks of immune activation, insertional mutagenesis, or vector immunity may be increased with repeat dosing
        iii. Treatment with an Additional or Other Gene/Cellular Therapy
            1. Treatment with an additional or different gene or cellular therapy after prior exposure to any gene or cellular therapy is also considered experimental and investigational, unless supported by evidence demonstrating (a-c):
                a. Anticipated clinical benefit beyond available standard therapies
                b. Safety of sequential administration
                c. Justification for selecting a second gene/cellular intervention after a prior one
            2. This includes, but is not limited to:
                a. Switching between CAR-T products (e.g., CD19 → CD19 or CD19 → BCMA)
                b. Switching between autologous and allogeneic cellular therapies
                c. Sequential use of CAR-T, TCR-T, NK-cell therapies, or other genetically engineered cell therapies
                d. Receiving a gene therapy after previous gene or cellular therapy exposure
                e. Receiving an in vivo gene therapy following any prior vector-based therapy
        iv. Prior Gene/Cell Therapy Exposure
            1. An individual is generally not eligible for additional gene or cellular therapy if they have previously received:
                a. Any autologous cellular therapy (e.g., CAR-T, TCR-T, TIL),
                b. Any allogeneic genetically modified cellular therapy,
                c. Any in vivo gene therapy (e.g., AAV, lentiviral vector)
                d. Any ex vivo gene-modified cell product

e. Are being considered for any other gene or cellular therapy without documented evidence supporting safety and anticipated benefit.

CODES:

Eligibility for reimbursement is based upon the benefits set forth in the member's subscriber contract. CODES MAY NOT BE COVERED UNDER ALL CIRCUMSTANCES. PLEASE READ THE POLICY AND GUIDELINES STATEMENTS CAREFULLY.

Codes may not be all inclusive as the AMA and CMS code updates may occur more frequently than policy updates.

Code Key:
Experimental/Investigational = (E/I),
Not medically necessary/ appropriate = (NMN).

HCPCS:

J3590 (NOC)

UPDATES:

Date	Revision
09/24/2026	Created & Implemented
08/13/2026	Review / P&T Committee Approval

REFERENCES:

1. National Organization for Rare Disorders – Leukocyte Adhesion Deficiency Syndromes. Updated March 14, 2018. Available at: https://rarediseases.org/rare-diseases/leukocyte-adhesion-deficiency-syndromes/#causes
2. A Clinical Trial to Evaluate the Safety and Efficacy of RP-L201 in Subjects With Leukocyte Adhesion Deficiency-I. ClinicalTrials.gov. Available at: https://clinicaltrials.gov/study/NCT03812263?intr=RP-L201&rank=1
3. Rocket Pharmaceuticals Announces Update on FDA Review Timeline of KRESLADI™ (marnetegragene autotemcel) for the Treatment of Severe Leukocyte Adhesion Deficiency-I (LAD-I). Published February 13, 2024. Available at: https://www.biospace.com/article/releases/rocket-pharmaceuticals-announces-update-on-fda-review-timeline-of-kresladi-marnetegragene-autotemcel-for-the-treatment-of-severe-leukocyte-adhesion-deficiency-i-lad-i-/
4. Kresladi [prescribing information]. Rocket Pharmaceuticals, Inc. Cranbury, NJ